Risk of Lung Cancer From Exposure to Dusts and Fibers in Leningrad Province, Russia

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Background *Exposures to several dusts and fibers (DFs) have been established or suggested as etiologic factors for lung cancer.*
Methods *To investigate lung cancer risk in relation to exposure to DFs, we identified 540 pathologically-diagnosed lung cancer cases and 582 controls from the 1993–1998 autopsy records of the 88 hospitals of Leningrad Province, Russia. Lifetime job-specific exposure measurements were available for 15 organic, 15 man-made and 28 natural-inorganic agents.*
Results *In male workers, increased risks were found for linen dust (OR = 3.68, 95% CI 1.00–13.6, adjusted for age, smoking and residence), and unspecified DFs (OR = 1.44, 95% CI 1.07–1.94). Small non-significant excess risks were observed for quartz dust (OR = 1.27; 95% CI 0.83–1.93) and man-made vitreous fibers (MMVFs) (OR = 1.82, 95% CI 0.88–3.75). In female subjects, risks were non-significantly associated with paper dust (OR = 1.77, 95% CI 0.74–4.20), and unspecified DFs (OR = 1.52, 95% CI 0.77–3.03).*
Conclusions *The study showed increased lung cancer risk for selected categories of DFs.*
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KEY WORDS: glass wool; linen dust; man-made vitreous fibers; occupation; paper dust; particles; quartz

INTRODUCTION

Lung cancer is the most frequent malignant neoplasm and cause of death from neoplasia in several countries, including Russia. Several dusts and fibers (DFs), such as crystalline silica, nickel ore dust and asbestos, have been classified by the International Agency for Research on Cancer (IARC) as carcinogens to humans [Boffetta and Trichopoulos, 2002; Siemiatycki et al., 2004]. Associations with lung cancer risk have been suggested, but not conclusively demonstrated, for wood, paper, grain, coal, ferric oxide, cement, limestone, and clay dusts, as well as for Man-Made Vitreous Fibers (MMVFs) [Waxweiler et al., 1988; Siemiatycki et al., 1989; Blot and Fraumeni, 1996; Monson, 1996; Weston et al., 2000; Boffetta and Trichopoulos, 2002]. A case-control study was conducted in Leningrad Province, Russia to investigate the association of lung cancer risk with exposure to DFs.

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MATERIALS AND METHODS

Study Subjects

In Leningrad Province, an industrialized area with a population of 1.5 million subjects, autopsy examinations are performed on approximately 95% of the subjects who die in the 88 local state hospitals. From 1993–1998 autopsy records of the St. Petersburg Central Pathology Laboratory, which collects reports on all autopsies performed in the Province, we identified 540 pathologically diagnosed lung cancer cases (474 men and 66 women), and 582 controls (453 men and 129 women) selected from deceased subjects with autopsy-based diagnosis of non-cancer and non-smoking-related diseases. Controls who died from smoking-related diseases were excluded because these diagnoses are likely to be indirectly associated with the exposure, given that specific dust exposures have been found to be more frequent among smokers [McCurdy et al., 2003]. Median age at death of lung cancer cases was 63 years (range: 33–86 years) for male and 68 years (range: 22–84 years) for female subjects. Controls were frequency matched to the cases by gender (using a case-control frequency proportion of 1:1 for males and 1:2 for females), age, region and year of death. The causes of death of the control subjects were: Infectious diseases (1.4%), diabetes and other pancreatic disorders (0.9%), anemia and other blood diseases (1.0%), diseases of the nervous system (15.3%), ischemic heart disease (7.9%), diseases of pulmonary circulation (4.8%), diseases of pericardium (2.2%), heart failure (33.0%), cerebrovascular disease (7.2%), other disorders of the circulatory system (0.5%), pneumonia and influenza (6.4%), other diseases of lung and respiratory system (0.7%), diseases of the digestive system (9.6%), diseases of the genitourinary system (3.4%), symptoms involving cardiovascular system (2.9%), injuries (0.3%), and other disorders and symptoms (2.4%). The manufacturing industry was the most frequent area of employment of the study subjects [Baccarelli et al., 2005]. We obtained health-related data, including information on smoking, from local health services and hygiene centers that routinely use standardized protocols to record them. Gender-specific proportions of smokers among control subjects were comparable to the reported prevalence of tobacco use in the Russian Federation [Baccarelli et al., 2005]. Among male controls, 43% of the subjects were light smokers (< one pack/day) and 37% were heavy smokers (one pack of cigarettes a day or more). Among female controls, 18 and 4% were light and heavy smokers, respectively. Among lung cancer cases, smoking prevalence was very high in males (42% light smokers and 55% heavy smokers) and lower in females (17% light and 11% heavy smokers) possibly reflecting lower smoking rates among females in this population, as well as underreporting by female subjects, given that, until recent years, smoking was not considered proper for women in Russia. The study protocol was reviewed and approved by the Institutional Review Board of the U.S. National Cancer Institute (NCI).

Exposure Assessment

Local hygiene centers have periodically and routinely obtained monitoring data from all the work facilities in Leningrad Province on 58 agents, including 15 organic, 15 man-made and 28 natural inorganic DFs. We reviewed the hygiene-center records to obtain specific exposure data for all the jobs held by the subjects in our study. For each subject, individual information on job-title, work-location, work-area, and start and end dates obtained from lifetime work history records were used to identify relevant exposure measurement data collected in the archives of the hygiene centers. Relevant exposure data, usually based on stationary measurements routinely performed to comply with hygiene regulations, were those performed in a work-area during the period a study subject had been working in it.

Exposure data were retrieved and evaluated by 17 occupational physicians (one from each of the regions in the province) with specific expertise in the assessment of historical workplace exposures. To ensure accurate and standardized exposure assessment procedures, the physicians received extensive training by an occupational hygienist from the NCI (M.D.). If data were unavailable or not sufficiently detailed at the hygiene centers, the physicians visited the employment site to obtain additional exposure information from the factory archives. Each exposure was classified with respect to its presence, intensity, frequency, and duration. For each exposure, a confidence score reflecting the degree of certainty in the information retrieved (from $1 = $ low to $4 = $ very high) was assigned. We used MAC values for respirable DFs [Maximum Allowable Concentrations (MACs, 1998) of Harmful Substances in Occupational Air. Hygiene standards 2.2.5., 1998] to standardize intensities across all potential exposures. The exposure intensity for a 40-hour work week was estimated on the basis of work-area measurements and categorized using the following score system: Non-exposure, score $= 0$; $<50\%$ of the MAC, score $= 0.25$; $=>50\%$ but $<100\%$ MAC, score $= 0.75$; and $=>100\%$ MAC, score $= 2.25$. The average intensity score of a specific exposure was calculated as the time-weighted mean of intensity scores. The cumulative exposure score was calculated as the product of average intensity score per total duration. For example, consider a worker exposed to Agent X on two different occasions: For 4 years at intensity $=>100\%$ MAC (intensity score $= 2.25$); and for 10 years at intensity $<50\%$ MAC (intensity score $= 0.25$). The worker would have the following metrics of exposure to X: Duration of 14 years, that is, $4 + 10$ years; average intensity of 0.82, that is, $((2.25 \times 4 \text{ years}) + (0.25 \times 10 \text{ years}))/14$ years; cumulative exposure score of 11.48, that is, 0.82×14 years. For the analysis, we categorized the average intensity scores into two groups: (a) <0.75 (i.e., $<75\%$ MAC); and (b) $=>0.75$ (i.e., $=>75\%$ MAC). For exposure groups including more than one single agent, mean durations, mean duration-weighted intensity scores, and mean cumulative exposure scores were used.

Statistical Analysis

Gender-specific Odds Ratios (ORs) and 95% confidence intervals (CIs) adjusted for age, smoking (never, not every day, <20 cigarettes/day, =>20 cigarettes/day) and region of residence (grouped in 5 geographic zones) using unconditional multiple logistic regression analysis are calculated. No major changes were observed when year of death or exposure to DFs carcinogenic to the lung (asbestos, talc, granite dust, and quartz dust) were included in the models, when subjects who had held high-risk jobs (welders, foundry workers, miners, metal workers, drivers, and chemical workers) [Baccarelli et al., 2005] were excluded from the analysis, or when a 10-year lag was used. ORs for lung cancer were calculated for exposures with five or more lung cancer cases. In the analyses stratified by smoking status, ORs were adjusted for age and region of residence for non-smokers; and by age, region of residence, and number of cigarettes/day for smokers. A *P*-value <0.05 was considered statistically significant. All the analyses were performed using Stata 8.0 (Stata Corp., College Station, TX).

RESULTS

Exposure to DFs (Ever/Never) and Risk of Lung Cancer

Most of the study subjects were exposed to one or more of the 58 DFs we evaluated. Overall, 422 cases (89.0%) and 397 controls (87.6%) among males, and 52 cases (78.8%) and 106 controls (82.2%) among females were ever exposed.

In male subjects (Table I), exposure to organic DFs was associated with an OR for lung cancer risk of 1.06 (95% CI 0.80–1.40, adjusted for age, smoking and region of residence). An increased risk was found among subjects exposed to linen dust (OR = 3.68, 95% CI 1.00–13.6), and, to a lesser extent, cotton dust (OR = 2.43, 95% CI 0.67–8.82). When we divided the study subjects by smoking habits, male non-smokers exposed to organic DFs (8 of 13 non-smoker cases and 42 of 90 non-smoker controls) exhibited an OR of 2.02 (95% CI 0.46–8.80) for lung cancer, while exposed smokers (243 of 458 smoker cases and 186 of 360 smoker controls) had an OR of 1.04 (95% CI 0.78–1.38). Interestingly, an increase in lung cancer risk, though not significant, was observed among non-smokers exposed to wood dust (OR = 2.93, 95% CI 0.66–13.0, based on 4 cases and 12 controls), but not among smokers (OR = 1.00, 95% CI 0.71–1.40, based on 108 cases and 85 controls).

Male subjects exposed to man-made DFs exhibited a slight, non-significant excess risk (OR = 1.26, 95% CI 0.87–1.83). The highest relative odds were observed for workers exposed to MMVFs (OR = 1.82, 95% CI 0.88–3.75), including glass wool (OR = 1.77; 95% CI 0.57–5.51) and other MMVFs (OR = 3.34, 95% CI 1.18–9.45; other MMVFs included 2 cases and 1 control exposed to ceramic fibers; no cases and 3 controls exposed to slag wool; and 12 cases and 6 controls exposed to unspecified MMVFs). Four lung cancer cases exposed to MMVFs, but no controls, were also exposed to asbestos. However, when the analysis was adjusted for asbestos exposure, in addition to age, smoking, and region of residence, we still observed an association between MMVFs and lung cancer risk (OR = 1.72, 95% CI 0.83–3.89 for MMVFs; OR = 1.56, 95% 0.49–5.02 for glass wool; and OR = 3.25, 95% 1.16–9.11 for other MMVFs). Among non-smokers, the risks associated with man-made DFs (OR = 2.00, 95% CI 0.48–8.32, based on 4 cases and 15 controls) and MMVFs (OR = 5.42, 95% CI 0.59–49.7, based on 2 cases and 3 controls only) tended to be higher than among smokers (OR = 1.21, 95% CI 0.83–1.78 for man-made DFs, based on 80 cases and 57 controls; and OR 1.56, 95% CI 0.74–3.27 for MMVFs, based on 21 cases and 12 controls).

Exposure to natural inorganic DFs was associated with decreased lung cancer risk (OR = 0.59, 95% CI 0.44–0.79). A few male workers (6 cases and 4 controls) were ever exposed to asbestos (OR = 2.20, 95% CI 0.53–9.09). No overall excess risk was found for subjects exposed to silica-containing dust (OR = 0.75, 95% CI 0.57–0.99), but non-significant increased risks were found for exposure to quartz (OR = 1.27, 95% CI 0.83–1.93) and granolith dust, a mixture of crushed granite and cement (OR = 3.26, 95% CI 0.38–28.3).

We found a significant increase in lung cancer risk among male workers exposed to non-specified DFs (OR = 1.44, 95% CI 1.07–1.94).

Among women (Table II), workers exposed to organic DFs had an OR for lung cancer of 1.04 (95% CI 0.55–1.97), with a moderate, non-significant risk increase for exposure to paper dust (OR = 1.77, 95% CI 0.74–4.20), coal dust (OR = 1.47, 95% CI 0.41–5.24) or peat dust (OR = 1.48, 95% CI 0.47–4.63). No excess risk was associated with exposure to man-made DFs (OR = 1.03, 95% CI 0.52–2.02).

Similarly to men, female workers exposed to natural inorganic DFs had decreased relative odds for lung cancer (OR = 0.56, 95% CI 0.28–1.12). Also, a non-significant risk increase was observed among female subjects exposed to unspecified DFs (OR = 1.52, 95% CI 0.77–3.03).

Analysis by Duration, Average Intensity and Cumulative Exposure

We evaluated lung cancer risk by duration, average intensity and cumulative exposure score for the main groups of exposures and for the categories that showed increased risk in the ever/never analysis. Among male subjects (Table III), lung cancer risks tended to increase by intensity of exposure to man-made DFs (OR = 1.05, 95% CI 0.63–1.74 for MAC <75%; and OR = 1.50, 95% CI 0.91–2.47 for

TABLE I. Risk of Lung Cancer Associated With Exposure to Dusts and Fibers (DFs) in Male Subjects

Exposure	Case (n = 474)	Control (n = 453)	OR[a]	(95% CI)[a]
Organic dusts and fibers	253	230	1.06	(0.80–1.40)
Wood dust	113	97	1.05	(0.75–1.46)
Coal dust	64	57	1.01	(0.67–1.51)
Grain dust	50	48	0.94	(0.60–1.46)
Non-grain agricultural dust	32	22	1.24	(0.68–2.26)
Flour dust	10	10	1.08	(0.40–2.89)
Peat dust	32	29	1.09	(0.62–1.91)
Paper dust	10	23	0.47	(0.21–1.04)
Wool dust	15	13	1.05	(0.47–2.38)
Linen dust	10	4	3.68	(1.00–13.6)
Cotton dust	8	4	2.43	(0.67–8.82)
Leather dust	5	4	0.70	(0.17–2.86)
Other organic dusts and fibers[b,c]	3	8	—	—
Man-made dusts and fibers	85	72	1.26	(0.87–1.83)
Man-made vitreous fibers (MMVFs)	23	15	1.82	(0.88–3.75)
Glass wool	10	5	1.77	(0.57–5.51)
Other MMVFs	14	7	3.34	(1.18–9.45)
Abrasive dust	55	44	1.35	(0.86–2.13)
Plastic dust	6	6	0.78	(0.22–2.51)
Other man-made dusts and fibers[b]	19	16	1.22	(0.59–2.54)
Natural inorganic dusts and fibers	299	325	0.59	(0.44–0.79)
Silica-containing dusts	212	219	0.75	(0.57–0.99)
Quartz dust	67	46	1.27	(0.83–1.93)
Cement dust	59	62	0.85	(0.56–1.27)
Granite dust	14	12	1.09	(0.46–2.59)
Granolith dust	6	1	3.26	(0.38–28.3)
Unspecified	151	160	0.77	(0.58–1.04)
Silicate-containing dust	57	79	0.61	(0.41–0.90)
Limestone	17	15	1.05	(0.48–2.30)
Shale dust	16	16	1.12	(0.50–2.50)
Clay	8	12	0.58	(0.22–1.55)
Asbestos	6	4	2.20	(0.53–9.09)
Metal dusts	149	153	0.92	(0.68–1.25)
Iron oxide	88	85	1.03	(0.72–1.47)
Manganese oxides	41	39	1.00	(0.61–1.64)
Chromium oxides	23	33	0.63	(0.35–1.14)
Aluminum oxide	10	11	0.98	(0.35–2.73)
Bauxite	5	7	0.86	(0.22–3.34)
Vanadium pentaoxide	8	7	0.97	(0.33–2.83)
Unspecified	90	103	0.78	(0.56–1.10)
Other metal dusts[b]	5	4	1.39	(0.33–5.95)
Other natural inorganic dusts and fibers[b]	13	16	0.85	(0.38–1.88)
Dusts and fibers, unspecified	179	136	1.44	(1.07–1.94)

OR = odds ratio, 95% CI = 95% confidence interval.
[a]Adjusted for age, smoking and region of residence in multiple logistic regression analysis.
[b]Category including exposures with less than 5 lung cancer cases.
[c]Odds ratios and 95% confidence intervals were not calculated for exposure categories with less than five lung cancer cases.

TABLE II. Risk of Lung Cancer Associated With Exposure to Dusts and Fibers in Female Subjects

Exposure	Case (n = 66)	Control (n = 129)	OR[a]	(95% CI)[a]
Organic dusts and fibers	35	70	1.04	(0.55–1.97)
Wood dust	7	20	0.79	(0.30–2.07)
Coal dust	5	7	1.47	(0.41–5.24)
Non-grain agricultural dust	5	15	0.70	(0.24–2.08)
Peat dust	6	10	1.48	(0.47–4.63)
Paper dust	12	16	1.77	(0.74–4.20)
Cotton dust	6	9	1.34	(0.42–4.22)
Other organic dusts and fibers[b]	13	39	0.58	(0.28–1.22)
Man-made dusts and fibers	20	43	1.03	(0.52–2.02)
Man-made vitreous fibers (MMVFs)[c]	2	9	—	—
Synthetic detergents	16	32	1.11	(0.54–2.31)
Other man-made dusts and fibers[b,c]	3	10	—	—
Natural inorganic dusts and fibers	20	55	0.56	(0.28–1.12)
Silica-containing dusts	15	48	0.44	(0.21–0.93)
Metal dusts	9	14	1.34	(0.50–3.59)
Iron oxide	6	6	2.21	(0.63–7.80)
Other metal dusts[b]	6	8	1.75	(0.53–5.82)
Other natural inorganic dusts and fibers[b]	7	16	1.04	(0.38–2.84)
Dusts and fibers, unspecified	22	33	1.52	(0.77–3.03)

OR = odds ratio, 95% CI = 95% confidence interval.
[a]Adjusted for age, smoking and region of residence in multiple logistic regression analysis.
[b]Category including exposures with less than 5 lung cancer cases.
[c]Odds ratios and 95% confidence intervals were not calculated for exposure categories with less than five lung cancer cases.

MAC = >75%), MMVFs (OR = 1.36, 95% CI 0.49–3.79 for MAC <75%; and OR = 2.38, 95% CI 0.86–6.57 for MAC = 7>75%), or glass wool (OR = 0.83 95% CI 0.16–4.18 for MAC<75%; and OR = 3.61, 95% CI 0.64–20.4 for MAC = >75%). The MAC value for glass wool was equal to 2 mg/m^3. The intensity score for man-made DFs, and for MMVFs, which included multiple agents, was calculated as an average composite index reflecting the concentration, relative to its MAC value, of each single agent.

A non-significant risk increase was present among male subjects exposed to quartz dust at higher intensity (OR = 1.48, 95% CI 0.89–2.46 for MAC = >75%; Quartz MAC value = 1 mg/m^3). Only three cases and no controls had been exposed to asbestos at intensity = >75% MAC (Asbestos MAC value = 2 mg/m^3). A significant risk increase was observed among male workers exposed to unspecified DFs for 10 years or longer (OR = 1.53, 95% CI 1.09–2.15).

Among female subjects exposed to paper dust (Table III), lung cancer risk was elevated in those individuals who had been exposed for 10 years or longer (OR = 2.53, 95% CI 0.97–6.61) and tended to increase by cumulative exposure score (OR = 1.17, 95% CI 0.35–3.93 for score <5 OR = 2.58, 95% CI 0.82–8.11 for score = >5). Risks associated with exposure to natural inorganic DFs, including silica-containing dusts, showed a negative trend among female subjects by duration, average intensity score, and cumulative exposure score (Table III). For several other exposures, usually involving relatively few subjects, no consistent relationship was found with duration, average intensity or cumulative exposure score.

In all analyses, we obtained similar results when exposure data with low confidence scores were excluded (data not shown).

DISCUSSION

The present case-control study showed increased lung cancer risks among male workers exposed to linen dust or unspecified DFs. Among men exposed to MMVFs a moderate, non-significant overall excess risk, which tended to increase at higher exposure intensity was found. The same was found among women exposed to paper dust or unspecified DFs, when correlated with cumulative exposure. Other agents showed a moderate association with lung cancer, but with no additional supporting evidence from the duration- and intensity-based analyses.

The increased risk observed among subjects exposed to linen and, to a lesser extent, cotton dust, may be related to the high lung cancer rates among textile workers reported in other previous investigations [Blot and Fraumeni, 1996]. Those investigations were conducted in developing countries

TABLE III. Risk of Lung Cancer by Duration, Average Intensity and Cumulative Exposure to Selected Dusts and Fibers

	Duration		Average intensity		Cumulative exposure score	
	<10 years	=> 10 years	<75% MAC[a]	>= 75% MAC[a]	<5[b]	=>5[b]
Exposure	OR (95% CI)[c]	OR (95% CI)[c]	OR (95% CI)[c]	OR (95% CI)[c]	OR (95% CI)[c]	OR (95% CI)[c]
Males						
Organic dusts and fibers	1.19 (0.82–1.71)	0.99 (0.72–1.36)	1.04 (0.70–1.54)	1.07 (0.79–1.46)	1.29 (0.88–1.89)	0.95 (0.70–1.30)
Cotton dust	10.10 (1.02–100.2)	0.65 (0.10–4.10)	4.04 (0.67–24.4)	1.32 (0.21–8.10)	—	0.23 (0.03–2.17)
Linen dust	3.58 (0.83–15.4)	4.09 (0.24–68.8)	4.20 (0.26–69.3)	3.55 (0.83–15.3)	3.54 (0.63–19.8)	3.87 (0.54–27.5)
Man-made dusts and fibers	1.71 (0.94–3.10)	1.07 (0.69–1.67)	1.05 (0.63–1.74)	1.50 (0.91–2.47)	1.60 (0.89–2.86)	1.10 (0.70–1.72)
Man-made vitreous fibers (MMVFs)	4.32 (1.21–15.4)	1.11 (0.46–2.69)	1.36 (0.49–3.79)	2.38 (0.86–6.57)	3.22 (1.00–10.4)	1.23 (0.49–3.07)
Glass wool	—	1.20 (0.36–4.02)	0.83 (0.16–4.18)	3.61 (0.64–20.4)	1.79 (0.16–20.2)	1.77 (0.49–6.36)
Other MMVFs	3.66 (0.98–13.7)	0.99 (0.27–3.60)	2.09 (0.59–7.47)	1.81 (0.51–6.48)	4.01 (1.10–16.6)	0.78 (0.20–3.07)
Natural inorganic dusts and fibers	0.65 (0.42–0.98)	0.57 (0.42–0.78)	0.63 (0.44–0.90)	0.56 (0.40–0.78)	0.59 (0.38–0.92)	0.59 (0.43–0.80)
Silica-containing dusts	0.80 (0.52–1.22)	0.73 (0.54–0.99)	0.76 (0.51–1.12)	0.75 (0.54–1.02)	0.72 (0.46–1.14)	0.76 (0.56–1.02)
Quartz dust	1.64 (0.79–3.40)	1.13 (0.69–1.85)	0.93 (0.47–1.86)	1.48 (0.89–2.46)	1.50 (0.70–3.20)	1.18 (0.73–1.92)
Asbestos	2.38 (0.42–13.5)	1.87 (0.17–21.1)	1.13 (0.21–6.06)	—	2.38 (0.42–13.5)	1.87 (0.17–21.1)
Metal dusts	0.87 (0.54–1.41)	0.94 (0.67–1.33)	1.07 (0.71–1.62)	0.83 (0.57–1.19)	0.82 (0.50–1.36)	0.96 (0.69–1.35)
Dusts and fibers, unspecified	1.27 (0.80–2.01)	1.53 (1.09–2.15)	1.66 (1.05–2.65)	1.35 (0.96–1.89)	1.32 (0.78–2.24)	1.05 (0.68–1.61)
Females						
Organic dusts and fibers	0.88 (0.33–2.36)	1.11 (0.55–2.21)	1.35 (0.64–2.83)	0.78 (0.35–1.72)	1.25 (0.48–3.24)	0.97 (0.48–1.95)
Coal dust	2.01 (0.25–16.3)	1.25 (0.27–5.89)	1.24 (0.18–8.58)	1.66 (0.33–8.37)	1.90 (0.34–10.6)	1.12 (0.19–6.77)
Peat dust	2.66 (0.45–15.7)	1.01 (0.23–4.49)	0.68 (0.06–7.87)	1.87 (0.52–6.72)	4.01 (0.54–29.5)	0.91 (0.21–3.86)
Paper dust	0.41 (0.05–3.60)	2.53 (0.97–6.61)	2.58 (1.01–6.59)	—	1.17 (0.35–3.93)	2.58 (0.82–8.11)
Man-made dusts and fibers	0.68 (0.24–1.95)	1.28 (0.59–2.81)	1.50 (0.68–3.28)	0.52 (0.18–1.54)	0.55 (0.18–1.70)	1.39 (0.64–3.03)
Natural inorganic dusts and fibers	1.02 (0.40–2.60)	0.37 (0.15–0.88)	0.80 (0.33–1.91)	0.40 (0.16–0.98)	0.97 (0.39–2.40)	0.37 (0.15–0.89)
Silica-containing dusts	0.77 (0.29–2.03)	0.28 (0.10–0.75)	0.62 (0.22–1.76)	0.36 (0.15–0.88)	0.58 (0.21–1.61)	0.36 (0.15–0.91)
Metal dusts	17.1 (1.74–167)	0.44 (0.11–1.74)	2.07 (0.57–7.49)	0.8 (0.19–3.44)	4.22 (0.92–19.3)	0.58 (0.14–2.31)
Dusts and fibers, unspecified	1.53 (0.43–5.46)	1.52 (0.72–3.21)	2.29 (0.97–5.41)	0.98 (0.36–2.66)	1.30 (0.38–4.47)	1.69 (0.79–3.62)

OR = odds ratio, 95% CI = 95% confidence interval.
[a]MAC = Maximum Allowable Concentration. MAC values for single agents reported in the table were the following: Cotton dust, 2 mg/m^3; Linen dust, 2 mg/m^3; Glass wool, 2 mg/m^3; Quartz dust, 1 mg/m^3; Asbestos, 2 mg/m^3; Coal dust, 6 mg/m^3; Peat dust, 4 mg/m^3; Paper dust, 2 mg/m^3. For exposure categories including more than one agent, intensity represents the average of individual intensity scores.
[b]Cumulative exposure score was calculated as the product of average intensity score (ranging from 0.25 to 2.25) per total duration.
[c]Adjusted for age, smoking and region of residence in multiple logistic regression analysis.

or included subjects with concurrent asbestos exposure [Blot and Fraumeni, 1996; Chiappino et al., 2003]. However, other studies have described a decreased lung cancer risk in workers exposed to cotton or other agricultural dusts [Blot and Fraumeni, 1996]. In our study none of the workers exposed to linen or cotton dust were exposed to asbestos suggesting that our finding may not reflect a spurious association.

The involvement of MMVFs in the causation of lung cancer is still being debated [Boffetta and Trichopoulos, 2002]. In our study, male subjects exposed to MMVFs exhibited an increased, though not significant, lung cancer risk. The risks estimated in our study were higher than those reported by a meta-analysis indicating that glass and rock wool exposure is associated with lung cancer [Berrigan, 2002]. We also evaluated whether our findings could have been produced by the presence of asbestos exposure in the same subjects. Multivariable models adjusted for exposure to asbestos confirmed the presence of an association between MMVFs and lung cancer risk in our data.

In female subjects, we found a moderate increased risk among workers exposed to paper dust, consistent with the results of some [Toren et al., 1991; Blot and Fraumeni, 1996; Monson, 1996, Rix et al., 1997], but not other [Blot and Fraumeni, 1996; Langseth and Andersen, 2000; Szadkowska-Stanczyk and Szymczak, 2001] previous investigations on pulp and paper workers. Among both male and female workers, exposure to non-specified DFs was associated with a 50% increased risk of lung cancer. This exposure category included DFs that were poorly characterized and possibly contained a relatively high proportion of carcinogenic substances. It is unclear which agents may have played a role in determining the excess risk observed.

We found lower lung cancer risk for exposure to natural inorganic DFs, as well as to silica-containing dusts in general. This result raises the question on whether a healthy hire/survivor effect could have been present in our study and led to an underestimation of the risks associated with natural inorganic DFs. Although it is often retained that the healthy worker effect has little influence on the occurrence of cancer, the work by Sterling and Weinkam [1986] suggests that it is observed for all causes of death, including lung cancer. Nonetheless, male workers exposed to quartz dust exhibited a slight excess of lung cancer risk that, although not significant, was comparable to the effect size reported by previous investigations [Blot and Fraumeni, 1996; IARC, 1997; McDonald et al., 2001], as well as by a recent meta-analysis [Steenland et al., 2001]. Additionally, we found elevated relative odds of lung cancer in a small group of subjects exposed to granolith dust, a silica-containing mixture of crushed granite and cement often used as paving stone.

The present study is unique in that it was based on autopsy lung cancer cases and controls who died in the hospitals of Leningrad region. Because the subjects' selection was conducted using records from the St. Petersburg Central Pathology Laboratory archives, all cases had reliable lung cancer diagnoses based on pathology reports. Individual exposures to an extensive list of agents, including 58 DFs were assessed. To the best of our knowledge, this is the first case-control study to include measurements of such an extensive number of DFs. One of the recurrent weaknesses of case-control studies stems from the difficulty of retrospectively assessing past occupational exposures, which are often assumed only on the basis of job title by means of job-exposure matrices. In this study, we had the advantage of work-area measurements that were examined by highly qualified industrial hygiene specialists who were familiar with each local workplace and were specifically trained for the study to guarantee standardized procedures for exposure data retrieval and classification. In addition, the availability of exposure measurements over a wide time span allowed us to reconstruct lifetime exposure profiles for each of the study subjects and to conduct time- and intensity-based analyses. Exposure intensity for usual conditions of exposure during a 40-hour work week was classified on the basis of Russian MAC values, which tend to be higher than threshold values used in other countries. For instance, the MAC value for quartz in our study was equal to 1 mg/m^3, which is substantially higher than the MAK of 0.15 mg/m^3 set by the Deutsche Forschungsgeneinschaft [DFG, 1999]. For other exposures, however, the difference was not that significant (e.g., for cotton dust: Russian MAC value, 2 mg/m^3; DFG's MAK, 1.5 mg/m^3). For a number of agents, including some with known or suggested lung carcinogenicity (e.g., asbestos), the analysis was limited by the small number of observations, particularly for data from female subjects, and for data on duration, average intensity, and cumulative exposure. Also, the possibility of chance findings due to multiple comparisons cannot be excluded, thus, our results should be interpreted with caution. A limitation of the study is the lack of information on histological type of lung cancer. This limits our ability to capture histology-specific lung cancer risk by DF exposures. We are in process to obtain histological information on lung cancer to overcome this limitation.

In conclusion, occupational exposure to DFs was common in the study area. The present investigation showed increased risks of lung cancer for exposure to specific DFs. Our findings need to be appraised in the context of biological plausibility and evidence from other investigations conducted in different populations and study settings.

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REFERENCES

Baccarelli A, Khmelnitskii O, Tretiakova M, Gorbanev S, Lomtev A, Klimkina I, Tchibissov V, Averkina O, Dosemeci M. 2005. Occupation and lung cancer risk in Leningrad Province, Russia. Med Lav 96:142–154.

Berrigan D. 2002. Respiratory cancer and exposure to man-made vitreous fibers: A systematic review. Am J Ind Med 42:354–362.

Blot W, Fraumeni JF, Jr. 1996. Cancers of the lung and pleura. In: Fraumeni JF, Jr., Schottenfeld D, editors. Cancer epidemiology and prevention, 2nd edition. New York: Oxford University Press. p 637–665.

Boffetta P, Trichopoulos D. 2002. Cancer of the lung, larynx, and pleura. In: Adami HO, Hunter D, Trichopoulos D, editors. Textbook of cancer epidemiology. New York: Oxford University Press. p 248–280.

Chiappino G, Mensi C, Riboldi L, Rivolta G. 2003. Asbestos risk in the textile industry: Final confirmation of data from the Lombardy Mesothelioma Registry. Med Lav 94:521–530.

Deutsche Forschungsgemeinschaft. 1999. List of MAK and BAT values. Weinhem: VCH Verlagsgesellschaft.

IARC. 1997. Silica, some silicates, coal dust and para-aramid fibrils. Lyon: IARC Press.

Langseth H, Andersen A. 2000. Cancer incidence among male pulp and paper workers in Norway. Scand J Work Environ Health 26:99–105.

Maximum Allowable Concentrations (MACs) of Harmful Substances in Occupational Air. 1998. Hygiene Standards 2.2.5. 1998. (in Russian) Moscow. 137–139 p.

McCurdy SA, Sunyer J, Zock JP, Anto JM, Kogevinas M. 2003. Smoking and occupation from the European Community Respiratory Health Survey. Occup Environ Med 60:643–648.

McDonald AD, McDonald JC, Rando RJ, Hughes JM, Weill H. 2001. Cohort mortality study of North American industrial sand workers. I.

Mortality from lung cancer, silicosis and other causes. Ann Occup Hyg 45:193–199.

Monson RR. 1996. Occupation. In: Fraumeni JF, Jr., Schottenfeld D, editors. Cancer epidemiology and prevention, 2nd edition. New York: Oxford University Press. p 373–405.

Rix BA, Villadsen E, Lynge E. 1997. Cancer incidence of sulfite pulp workers in Denmark. Scand J Work Environ Health 23:458–461.

Siemiatycki J, Dewar R, Lakhani R, Nadon L, Richardson L, Gerin / SNM> M. 1989. Cancer risks associated with 10 inorganic dusts: Results from a case-control study in Montreal. Am J Ind Med 16:547–567.

Siemiatycki J, Richardson L, Straif K, Latreille B, Lakhani R, Campbell S, Rousseau MC, Boffetta P. 2004. Listing occupational carcinogens. Environ Health Perspect 112:1447–1459.

Steenland K, Mannetje A, Boffetta P, Stayner L, Attfield M, Chen J, Dosemeci M, DeKlerk N, Hnizdo E, Koskela R, Checkoway H. 2001. Pooled exposure-response analyses and risk assessment for lung cancer in 10 cohorts of silica-exposed workers: an IARC multicentre study. Cancer Causes Control 12:773–784.

Sterling TD, Weinkam JJ. 1986. Extent, persistence, and constancy of the healthy worker or healthy person effect by all and selected causes of death. J Occup Med 28:348–353.

Szadkowska-Stanczyk I, Szymczak W. 2001. Nested case-control study of lung cancer among pulp and paper workers in relation to exposure to dusts. Am J Ind Med 39:547–556.

Toren K, Sallsten G, Jarvholm B. 1991. Mortality from asthma, chronic obstructive pulmonary disease, respiratory system cancer, and stomach cancer among paper mill workers: A case-referent study. Am J Ind Med 19:729–737.

Waxweiler RJ, Zumwalde RD, Ness GO, Brown DP. 1988. A retrospective cohort mortality study of males mining and milling attapulgite clay. Am J Ind Med 13:305–315.

Weston TL, Aronson KJ, Siemiatycki J, Howe GR, Nadon L. 2000. Cancer mortality among males in relation to exposures assessed through a job-exposure matrix. Int J Occup Environ Health 6:194–202.